d l4 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:57374 CAPLUS
DN 140:107783
TI Method to reduce **false positive** outcomes in **prion** assays
IN Van Oers, Josephus W. A. M.; Van der Vorst, Teun J. K.; Hack, Cornelis E.; Van Engelenburg, Franciscus A. C.
PA Stichting Sanquin Bloedvoorziening, Neth.
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1382690	A1	20040121	EP 2002-77909	20020717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004067533	A1	20040408	US 2003-620082	20030715
WO 2004007761	A1	20040122	WO 2003-NL521	20030716
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI EP 2002-77909 A 20020717
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:574024 CAPLUS
DN 133:174276
TI **Prion** test using guanidine thiocyanate for reducing **false positive** test results
IN Garssen, Gerrit Jan; Jacobs, Jorg Gunther; Langeveld, Joannes Pieter Maria; Smits, Marinus Adrianus; Van Keulen, Lucien Johannes Mattheus; Schreuder, Bram Edward Cornelis; Bossers, Alexander
PA Stichting Dienst Landbouwkundig Onderzoek, Neth.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000048003	A1	20000817	WO 2000-NL79	20000209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, L				

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d his

     (FILE 'HOME' ENTERED AT 14:17:29 ON 17 JUN 2004)

     FILE 'MEDLINE' ENTERED AT 14:17:37 ON 17 JUN 2004
L1          4500 S PRION
L2         30270 S FALSE POSITIVE
L3             5 S L1 AND L2

     FILE 'CAPLUS' ENTERED AT 14:19:44 ON 17 JUN 2004
L4             2 S L1 AND L2

     FILE 'MEDLINE' ENTERED AT 14:20:44 ON 17 JUN 2004
                E TEUN J K/AU
                E HACK C E/AU
L5           326 S E3
L6             0 S PRION AND L5
L7             0 S FALSE POSITIVE AND L5
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d 13 1-5

L3 ANSWER 1 OF 5 MEDLINE on STN
AN 2004049423 MEDLINE
DN PubMed ID: 14687883
TI Proteinase K enhanced immunoreactivity of the **prion** protein-specific monoclonal antibody 2A11.
AU Brun Alejandro; Castilla Joaquin; Ramirez Miguel A; Prager Kai; Parra Beatriz; Salguero Francisco J; Shiveral Diane; Sanchez Carmen; Sanchez-Vizcaino Jose M; Douglas Alastair; Torres Juan M
CS Centro de Investigacion en Sanidad Animal, INIA, Ctra. Valdeolmos a El Casar sn, Valdeolmos, 28130 Madrid, Spain.
SO Neuroscience research, (2004 Jan) 48 (1) 75-83.
Journal code: 8500749. ISSN: 0168-0102.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040131
Last Updated on STN: 20040413
Entered Medline: 20040412

L3 ANSWER 2 OF 5 MEDLINE on STN
AN 2003344756 MEDLINE
DN PubMed ID: 12797926
TI [Use and validity of the 14-3-3 protein test in the diagnosis of **prion** diseases: a 4-year prospective study].
Utilizacion y validez de la prueba de la proteina 14-3-3 en el diagnostico de enfermedades por priones: estudio prospectivo de 4 anos.
AU Sanchez-Valle Diaz Raquel; Graus Ribas Francesc; Saiz Hinarejos Albert
CS Servicio de Neurologia. Institut Clinic de Malalties del Sistema Nervios. Instituto de Investigacion Biomedica August Pi i Sunyer (IDIBAPS). Hospital Clinic. Universidad de Barcelona. Barcelona. Espana.
SO Medicina clinica, (2003 May 31) 120 (20) 761-4.
Journal code: 0376377. ISSN: 0025-7753.
CY Spain
DT Journal; Article; (JOURNAL ARTICLE)
LA Spanish
FS Priority Journals
EM 200309
ED Entered STN: 20030725
Last Updated on STN: 20030925
Entered Medline: 20030924

L3 ANSWER 3 OF 5 MEDLINE on STN
AN 2001334298 MEDLINE
DN PubMed ID: 11402110
TI CSF detection of the 14-3-3 protein in unselected patients with dementia.
CM Comment in: Neurology. 2002 Feb 12;58(3):509-10. PubMed ID: 11839875
AU Burkhard P R; Sanchez J C; Landis T; Hochstrasser D F
CS Department of Neurology, University Hospital, Geneva, Switzerland.. Piere.Burkhard@hcuge.ch
SO Neurology, (2001 Jun 12) 56 (11) 1528-33.
Journal code: 0401060. ISSN: 0028-3878.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200107
ED Entered STN: 20010716
Last Updated on STN: 20020514

Entered Medline: 20010712

L3 ANSWER 4 OF 5 MEDLINE on STN
AN 2001180425 MEDLINE
DN PubMed ID: 11214920
TI Detection of PrP(Sc) in subclinical BSE with the paraffin-embedded tissue (PET) blot.
AU Schulz-Schaeffer W J; Fatzer R; Vandevelde M; Kretzschmar H A
CS Institute of Neuropathology, Georg-August University, Gottingen, Germany.
SO Archives of virology. Supplementum, (2000) (16) 173-80.
Journal code: 9214275. ISSN: 0939-1983.
CY Austria
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

L3 ANSWER 5 OF 5 MEDLINE on STN
AN 2000394378 MEDLINE
DN PubMed ID: 10833616
TI Creutzfeldt-Jakob disease: diagnostic utility of 14-3-3 protein immunodetection in cerebrospinal fluid.
AU Collins S; Boyd A; Fletcher A; Gonzales M; McLean C A; Byron K; Masters C L
CS The Australian Creutzfeldt-Jakob Disease Registry, Department of Pathology, the University of Melbourne, Victoria, Australia 3010.. s.colins@pathology.unimelb.edu.au
SO Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia, (2000 May) 7 (3) 203-8.
Journal code: 9433352. ISSN: 0967-5868.
CY SCOTLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000815

=> d l3 1-5 ab

L3 ANSWER 1 OF 5 MEDLINE on STN
AB Here, we report the development and further characterisation of a novel PrP-specific monoclonal antibody: 2A11. By Western blot analysis, 2A11 reacts with PrPC from a variety of species including cow, sheep, pig, hamster, rabbit, cat, dog, deer and mouse but fails to react with human, chicken and turtle PrP. Reactivity to PrPC in Western blot was found to be dependent on the redox state of the protein since binding of mAb 2A11 to its epitope was more effective in reducing conditions. 2A11 binding site was mapped within a region comprised by residues 171-179 (six octarepeats bovine PrP notation; 163-171 for the ovine PrP notation). Interestingly, in immunohistochemistry (IHC) analysis, immunoreactivity was greatly enhanced after proteinase K (PK) sample treatment, while little or no reaction was observed in non-PK-treated BSE samples and samples from healthy animals. Quantitative differences in reactivity to BSE prions after PK treatment were also observed, to a lesser extent, by Western blot analysis. Since definitive diagnosis of **prion**

diseases rely on IHC assays of proteinase K-treated samples, the use of mAb 2A11 might contribute to reduce the occurrence of **false positive** detection due to incomplete proteinase K digestion.

L3 ANSWER 2 OF 5 MEDLINE on STN

AB BACKGROUND AND OBJECTIVES: The 14-3-3 test shows a high efficiency for the diagnosis of Creutzfeldt-Jakob disease (CJD), as long as an appropriate clinical setting exists. We analyze the evolution of the use and the validity of this test in Spain. PATIENTS AND METHOD: From January 1997 to June 2001, 1,092 samples were tested in our laboratory; 674 samples were selected for the study. Diagnoses were obtained by the referring physicians and the national CJD surveillance system according to standard criteria (results of the test were not included). RESULTS: The number of samples analyzed (% of follow-up) was: 75 (96%) in 1997, 138 (82.3%) in 1998, 197 (73%) in 1999 and 264 (59%) in 2000. The negative predictive value, sensitivity and specificity for a diagnosis of **prion** disease revealed stable values (95, 86 and 86%, respectively). The positive predictive value (PPV) decreased from 77% in 1997 to 51% in 2000 because of an increase of **false-positive** (FP) results. Up to 25% of FP might have been excluded through neuroimaging or CSF characteristics. CONCLUSIONS: The observed increase of the demand suggests that the test is used as a screening technique. In this setting, the PPV of the test decreases due to an increase of **false-positive** results.

L3 ANSWER 3 OF 5 MEDLINE on STN

AB OBJECTIVE: To determine the usefulness of the 14-3-3 test in patients with dementia of various causes. BACKGROUND: Recent reports have suggested that the detection of the 14-3-3 protein in the CSF of patients with Creutzfeldt--Jakob disease is a highly sensitive and specific marker of the disease that might be used as a diagnostic criterion. We examined the validity of this test when applied to a cohort of unselected patients prospectively examined for an ongoing dementing process. METHODS: One hundred patients underwent an extensive neurologic examination for dementia, including a CSF 14-3-3 protein immunoblotting assay. Final clinical diagnoses were compared with the qualitative results of the test, and statistical measures of test validity were carried out. RESULTS: We found a positive test in 14 of 100 patients, only two of whom had definite Creutzfeldt--Jakob disease. Positive results were found in patients with various degenerative dementias, including AD (4), frontotemporal dementia (2), and dementia with Lewy body (1), and in patients with vascular dementia (1), carcinomatous meningitis (1), and anoxic encephalopathy (1). In two other positive patients, the dementia could not be confidently classified. Sensitivity, specificity, and negative predictive value were fairly good, but positive predictive value was poor. Similar results were found independently of the disease duration. There was no correlation between intensity nor pattern of the 14-3-3 protein expression and diagnosis. CONCLUSIONS: The 14-3-3 test is not valid for discriminating between Creutzfeldt--Jakob disease and non-Creutzfeldt--Jakob disease in unselected patients with dementia. Positive results are found in various degenerative and secondary, **prion**-unrelated dementias.

L3 ANSWER 4 OF 5 MEDLINE on STN

AB The appearance of a new variant of CJD (vCJD) in young patients has caused considerable public concern and there is evidence that this novel disease is caused by the same agent as BSE. BSE is a **prion** disease that became epidemic in the UK, with a peak incidence in January 1993. New test systems should aim to identify BSE-infected cattle early in the incubation period. We compared the established histological and immunohistochemical methods and the Western blot method used by Prionics with the PET blot method that detects **prion** PrP(Sc) deposits in formalin-fixed and paraffin-embedded tissue. Investigating the obex

region with the PET blot, all BSE cases were detectable and no **false positive** cases occurred. From the Swiss culling program, five clinically healthy cattle out of 1761 were identified as incubating BSE. With the PET blot method four of them showed the same PrP(Sc) deposition pattern that was seen in clinical BSE, though less conspicuous. In one of the five cases, PrP(Sc) was restricted to two brain stem nuclei, a pattern that was reported to be the first manifestation of PrP(Sc) deposits in the brain after peripheral infection and one that occurs after half of the incubation time. In this case, histology and Western blot were negative.

L3 ANSWER 5 OF 5 MEDLINE on STN

AB With the aim of improving the pre-mortem diagnostic accuracy of sporadic Creutzfeldt-Jakob disease (CJD), there has been considerable recent interest in the merit of immunodetecting 14-3-3 proteins in the cerebrospinal fluid (CSF) using Western blotting, with cumulative support for the utility of this technique. As a corollary, during a 20 month period, CSF samples from an unselected prospective series of 124 patients in whom sporadic CJD was a differential diagnostic possibility were examined by the Australian Creutzfeldt-Jakob disease Registry (ACJDR) for the presence of 14-3-3 proteins. Follow up to achieve a final diagnosis or clinical outcome was successful in 119. For definite and probable sporadic CJD combined, a positive result was 91.4% sensitive, while the sensitivity for the pathologically verified group alone was 96.0%. A negative outcome was 92.5% specific with **false positive** results seen in five patients with diagnoses which included inflammatory CNS disorders, cerebral ischaemia and dementia with Lewy bodies (DLB). Immunodetectable 14-3-3 proteins were present in three of four symptomatic patients with **prion** protein gene (PRNP) mutations. CSF samples containing significant amounts of blood were confirmed as suboptimal, with weak or qualitatively unusual positive results found in greater than 50% of such specimens, with only one of 14 such cases ultimately classified as definite or probable CJD.